Thyroid disorders

by Dr.Shadin alkatari

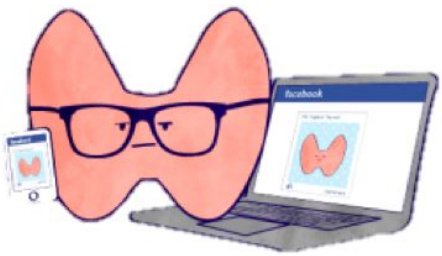
Note: Doctor said that the slide is more than enough for exam!

Done by: Asmaa AlRusaies

Revised by: Sarah Almubrik & Mohanad Alsuhaim

Objectives:

- **Thyroid anatomy and physiology**
- **Action of thyroid hormones**
- **Thyroid function Tests**
- **Thyroid disorders:**
- **Function Disorders:**
  a. **Hypothyroidism**
  b. **Hyperthyroidism**
- **Structure Disorders:**
  a. **Goiter**
  b. **Nodule**



References:

Slides - Black

Doctor's notes - Red

Step up / davidson - Blue

Extra explanation - Grey

Optional:

p738 to p757

❖ Anatomy of thyroid gland

- One gland has:
- 2 lobes, connected by the isthmus.
- Thyroid gland is made up of follicles.
- Weight 20 g, more in men, increase with age and body weight, decrease with iodine intake.
- Located in front of larynx.

❖ Thyroid histology

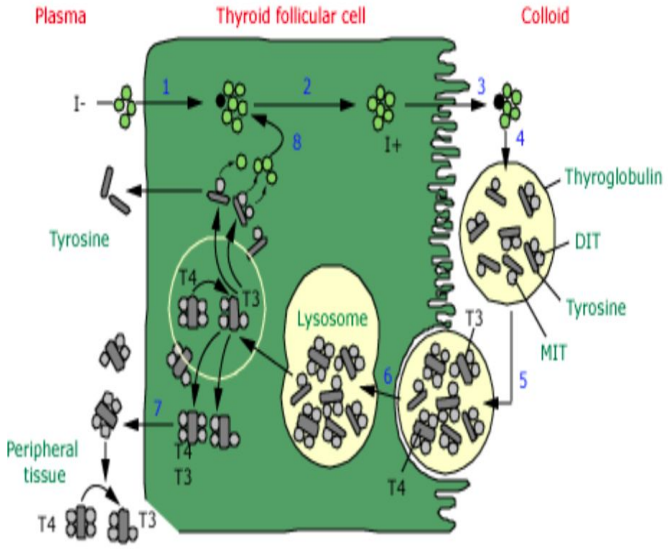
Click here

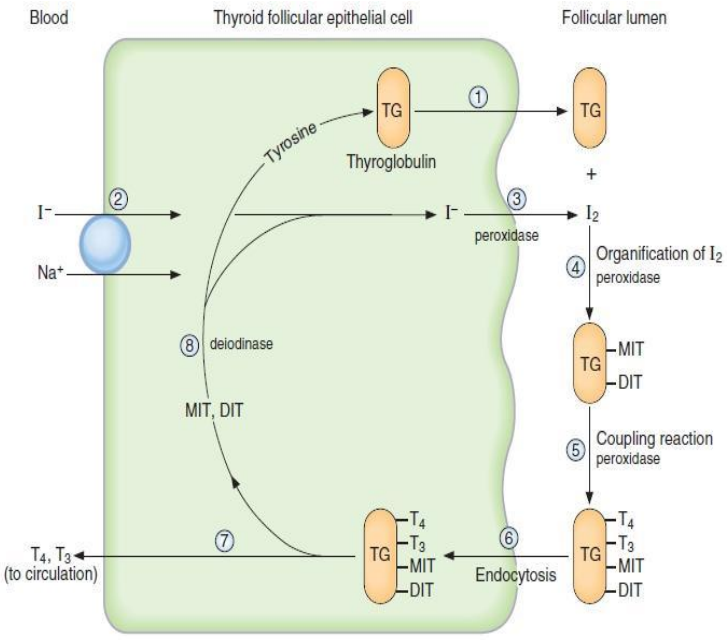
❖ Thyroid hormone action

- Thyroid hormones act on almost all the body systems.
- Somatic development in adults.
- Brain development in infant.
- Fetal thyroid functions at 10-12th weeks of gestation.
- Maternal T4 reaches the fetus during development , so if the mother has hypothyroidism :
  - Miscarriage.
  - Cognitive impairment of infant.
  - Preterm delivery.
- Main action of thyroid hormones is done by T3 "it's the active form which bound to the receptor":
  - 80% from peripheral conversion
  - 20% produced by the thyroid itself

❖ Thyroid hormones synthesis

- Follicular cells is the main site of thyroid hormones synthesis and storage
- Mainly T4 and small amount of T3
- Iodine is needed to produce the hormones
- Average body requirement of iodine is 150 mcg a day, 220 mcg for pregnant, 290 mcg for lactating. mcg = microgram
- Source of iodine: dairy and seafood products

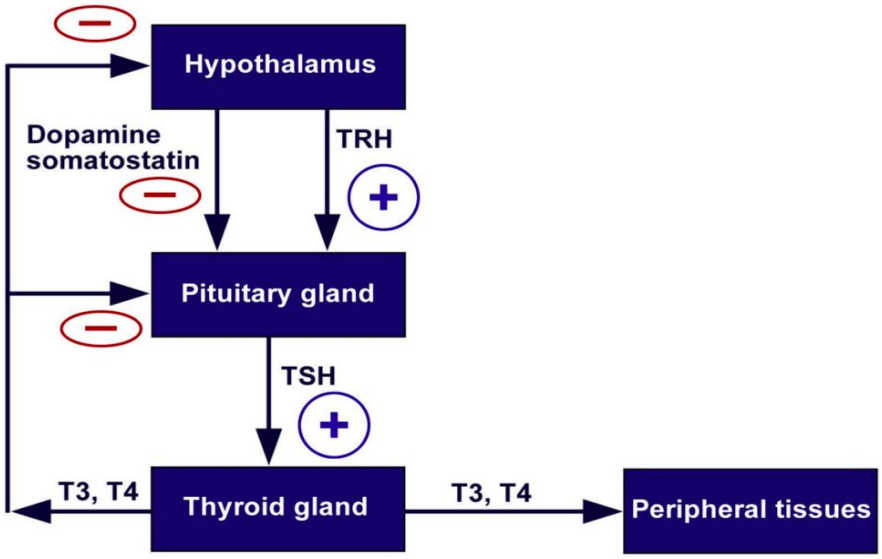


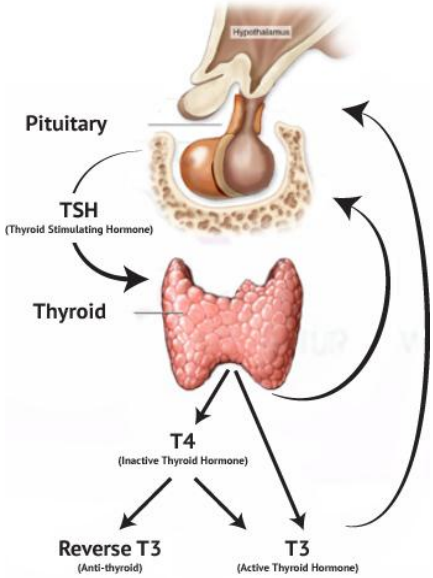


- Iodide is actively transported into follicular cell then into colloid
- organification & coupling are done by peroxidase enzyme

❖ Thyroid hormones:

- T4 and T3 synthesis and secretion is regulated by pituitary TSH
- TSH is inhibited by T4 and T3 (-ve feedback), stimulated by TRH
- Extrathyroidal conversion of T4 to T3 is regulated by nutrition, illness, hormonal factors
- 99.9% of T4 and T3 are bound to protein in the blood: TBG, albumin, lipoprotein



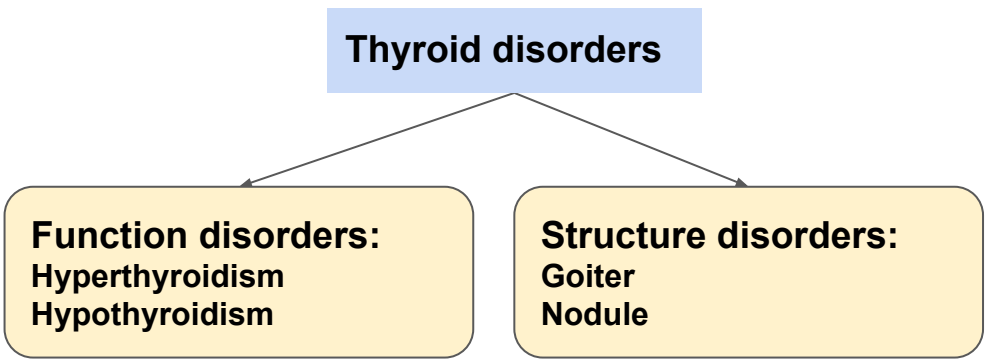


❖ Thyroid function tests (Biochemical):

- Thyroid function tests
  - Free T4
  - TSH
- Autoantibody tests:
  - Anti thyroid peroxidase Ab (Anti- TPO) = Most specific autoantibody test for autoimmune thyroiditis, high titer and it could be mildly elevated in normal person
  - TSI (TSH receptor Ab) = Specific for Graves disease

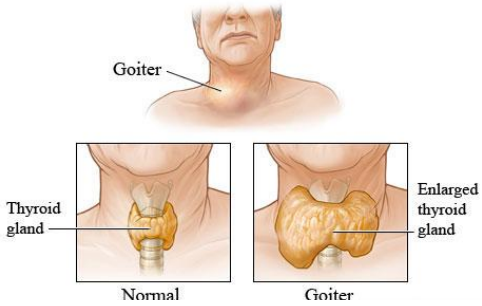
❖ Radiological imaging of thyroid (Anatomical) :

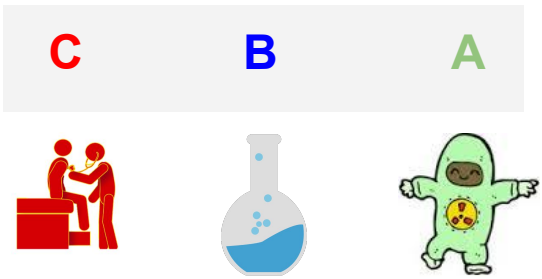
- US neck: The best radiological modality for assessment or suspected of structural thyroid disorders (nodule, goiter in eu or hypothyroid patient
- Radioactive uptake scan: To differentiate the cause of thyrotoxicosis ;
  - High uptake = active thyroid synthesis = (GD, toxic MNG, toxic adenoma)
  - No uptake = no active thyroid synthesis = thyroiditis, exogenous thyroid ingestion, ectopic thyroid tissue
- CT neck: sometimes for retrosternal goiter and compression symptoms



❖ Common thyroid disorders

- Goiter: chronic enlargement of thyroid gland.
- Endemic goiter: common in china and central africa.
- Sporadic goiter: multinodular goiter.
- Familia.
- Hashimoto's thyroiditis: in early stage.
- Grave's disease : due to chronic stimulation of TSH receptor.
- Diet : cabbage, cauliflower.
- Chronic iodine excess.
- Medication: lithium in 6%.
- Neoplasm.





C : clinical: History and examination of lump, hyper or hypothyroidism, compression symptoms, change in voice, family hx of thyroid tumors, hx of irradiation

B : Biochemical: TSH & T4

A : Anatomical

- **US neck : if patient with eu or hypothyroidism**
- **Radioactive uptake scan : thyrotoxicosis**

❖ Non-toxic Goiter:

- **Surgery (thyroidectomy) if:**
  - **Pressure symptoms**
  - **Malignancy**
  - **Cosmetic**

❖ Thyrotoxicosis

- **Hyperthyroidism: There are increase synthesis and release of thyroid hormones so, both T4,T3 will be high in same ratio**
  - **Thyroid uptake scan will be: high uptake (increased synthesis, need iodine)**
- **Non-Hyperthyroidism (other causes) : There are NO increase in synthesis of thyroid hormones, but increase of release of stored thyroid hormones in vesicles**
  - **so, T4>>T3**
  - **Thyroid uptake scan will be : low uptake (no increase synthesis)**

Sometimes, Thyrotoxicosis & Hyperthyroidism are used interchangeably

❖ C: Clinical

❑ History

- Sympathetic activation (nervousness, anxiety,increased perspiration,palpitation,...)
- Cardiovascular symptoms (SOB, atrial fib) and unexplained weight loss
- Ophthalmopathy (Graves disease)
- Hx of : Autoimmune disease, radiation, family hx, medication and dietary

❑ Examination

- Tachycardia or atrial arrhythmia, systolic hypertension with wide pulse pressure, warm, moist, smooth skin
- Lid lag, stare
- Hand tremor, muscle weakness
- Thyroid examination

Diffusely enlarged and slightly firm + bruit	• Graves disease (An autoimmune disorder, IgG binds to TSH receptor triggers the synthesis of excess thyroid hormone)
Enlarged (2-3 x) + soft	• MultiNodular Goiter (MNG)
Enlarged and painful	• subacute painful or granulomatous thyroiditis • degeneration or hemorrhage into a nodule and suppurative thyroiditis

- Ophthalmologic examination: 50% of GD have Graves Ophthalmopathy
  - periorbital edema
  - conjunctival edema (chemosis)
  - Injection
  - Poor lid closure
  - extraocular muscle dysfunction (diplopia)
  - proptosis

Note: Lid retraction (appearance of the upper scler) is seen with any hyperthyroidism, but proptosis (appearance of the lower sclera) is specific for Graves.

- dermatologic examination : Pretibial myxedema
  - deposition of glycosaminoglycans in the dermis of lower leg
  - nonpitting edema, erythema and thickening of the skin, without pain or pruritus
  - orange peel in color and texture

There are three signs of hyperthyroidism specific to Graves disease:

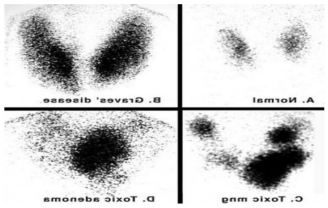
1-Exophthalmos 2-Pretibial myxedema 3-Thyroid bruit

❖ B: Biochemical

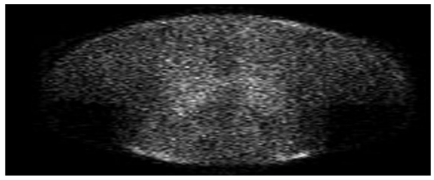
- Thyroid function tests
  - Free T4
  - TSH
- Autoantibody tests :
  - Anti- TPO : most specific autoantibody test for autoimmune thyroiditis
  - TSI (TSH receptor Ab) : only for Graves

❖ A: Anatomical

- Thyroid uptake scan :
  - Technetium-99m (99mTc)
  - Iodine-123 (123 I)



High uptake = active thyroid synthesis
(GD, toxic MNG, toxic adenoma)



No uptake = no active thyroid synthesis
(thyroiditis or exogenous)

❖ **Hyperthyroidism**: Hypermetabolic state caused by increased availability of thyroid hormones

❖ Hyperthyroidism with normal or high radioiodine uptake :

- Autoimmune thyroid disease (Graves , Hashitoxicosis)
- Autonomous thyroid tissue (toxic adenoma , toxic MNG)
- TSH - mediated hyperthyroidism
- Human chorionic gonadotropin mediated hyperthyroidism

❖ Hyperthyroidism with no radioiodine uptake :

- Thyroiditis
- Exogenous thyroid hormone intake (factitious hyperthyroidism)
- Ectopic hyperthyroidism (serum ovarii , metastatic follicular thyroid cancer)

❖ Clinical features of hyperthyroidism :

- **Skin:**
  - **warm, excessive sweating**
  - **Onycholysis, hyperpigmentation**
  - **Pruritus, vitiligo, alopecia, thinning of hair**
  - **pretibial myxedema**
- **Eyes:**
  - **common in Graves**
  - **extraocular muscle dysfunction : diplopia, proptosis, lid retraction, corneal ulceration, optic neuropathy and blindness**
  - **periorbital and conjunctival edema**
- **Cardiac:**
  - **Atrial fibrillation in 10-20%**
  - **High output cardiac failure**
  - **Wide pulse pressure, hypertension**
- **Respiratory:**
  - **Dyspnoea**
- **GI:**
  - **Weight loss, diarrhoea, increase liver enzyme**
- **Bone:**
  - **Bone turnover increased : osteoporosis**
- **Neuropsychiatry :**
  - **Behavioral and personality changes: irritability, depression**
- **Hyperactivity increased**

Three signs are specific to Graves disease:

- Exopthalmos
- Pretibial myxedema
- Thyroid bruit

Thyroid storm

is a life-threatening condition manifested by marked increase in the signs and symptoms of hyperthyroidism. "acute presentation"

Management:

- **IV fluid.** Supportive
- **Cooling blankets.** For high fever
- **Anti-thyroid agent (eg:PTU) .** every 2 hours in order to suppress thyroid
- **B-blockers.** To treat the tachycardia

❖ Lab-hyperthyroidism (Primary):

- **increased free T4** **increased free T3**
- **Low TSH.** **TSH-receptor antibodies**
- **increased radioactive iodine uptake on scan**

❖ Treatment of Graves disease

1- Thioamides

- **lower cost**
- **Minor S/E (**rash, GI, granulocytopenia) and major S/E
- **Major S/E (agranulocytosis, vasculitis "lupus-like syndrome", hepatitis)**
- **Risk of fetal goiter and hypothyroidism if pregnant**

2- Radioiodine

- **may cause permanent hypothyroidism**

3- Surgery

- **permanent hypothyroidism**
- **Risk of hypoparathyroidism, recurrent laryngeal nerve damage**

❖ Hypothyroidism "more common than hyperthyroidism"

❖ Primary hypothyroidism

- Chronic autoimmune thyroiditis "Hashimoto's thyroiditis"
- Iatrogenic (thyroidectomy, radiation therapy)
- Iodine deficiency or excess
- Drugs (thioamides, lithium, amiodarone)
- Infiltrative diseases (fibrous thyroiditis, hemochromatosis, sarcoidosis)
- Congenital thyroid agenesis

❖ Central hypothyroidism

- **TSH deficiency. (eg:** Sheehan's syndrome)
- **TRH deficiency**

❖ Generalized thyroid hormone resistance

!

Myxedema Coma

A rare condition that present with depressed state of consciousness, profound hypothermia, and respiratory depression.

Management:

- **IV thyroxine**
- **Hydrocortisone**
- **warming blankets.**

Subclinical Hypothyroidism:

- **Thyroid function is inadequate, but increased TSH production maintains T4 level within the reference range, TSH level is elevated and T4 level is normal**
- **Sub-clinical state is when there is highly increase in TSH with little or no decrease in T4 (TSH start to pickup change in T4 before the clinician notice)**
- **Look for nonspecific or mild symptoms of hypothyroidism, as well as elevated serum LDL lev**
- **Treat with thyroxine if patients develop goiter, hypercholesterolemia, symptoms of hypothyroidism, or significantly elevated TSH level (20 U/mL).**

The Dr did not mention it and not all drugs are written here

❖ Drugs affecting thyroid function or function tests:

❖ Drugs causing hypothyroidism :

- **Inhibition of thyroid hormone synthesis or release (thioamides, lithium, iodine, amiodarone)**
- **Decreased absorption of T4 (cholestyramine, iron sulfate, omeprazole)**
- **Immune Dysregulation (interferon-alpha, interleukin-2)**
- **Suppression of TSH (dopamine)**
- **Possible destructive thyroiditis (sunitinib)**
- **Increased T4 clearance & suppression of TSH (bexarotene)**

❖ Drugs causing hyperthyroidism :

- **Stimulation of thyroid hormone synthesis or release (iodine, amiodarone)**
- **Immune Dysregulation (interferon-alpha, interleukin-2)**

❖ Drugs causing abnormal thyroid function tests without thyroid dysfunction :

- **Increased T4 clearance (phenytoin, carbamazepine, rifampin, phenobarbital)**
- **Suppression of TSH secretion (dobutamine, glucocorticoids, octreotide)**
- **Impaired conversion of T4 to T3 (propylthiouracil, propanolol, nadol, amiodarone, glucocorticoids, contrast agent)**

❖ Major symptoms and signs of hypothyroidism :

Slowing of metabolic rate	→	**Fatigue, cold intolerance, dyspnea, weight gain, cognitive dysfunction, constipation,GF, bradycardia, delayed relaxation of reflexes, carotenemia**
Accumulation of matrix substances	→	**Dry skin, hoarseness, edema, coarse skin, puffy facies, loss of eyebrows, large tongue**
Other	→	**Decreased hearing, paresthesia, depression, menorrhagia, diastolic HTN, pleural and pericardial effusion, ascites, galactorrhea**

Note:

- almost all bodily processes being slowed down - except menstrual flow, which is increased (menorrhagia)
- Severe hypothyroidism causes myxedema, but hyperthyroidism is associated with pretibial myxedema

❖ Diagnosis:

- **High TSH**
- **LOW FREE T4 & T3**
- **Positive TPO antibodies**

❖ Treatment:

- ◇ **Thyroxine replacement (half life of T4 is one week, so we need 4-6 weeks before check T4, TSH to adjust thyroxine dose)**

Pattern of thyroid function tests during assessment of thyroid function

Assessment	Serum TSH	Serum Free T4	Serum T3
Normal hypothalamic- pituitary function			
Euthyriod	Normal	Normal	Normal
Euthyroid Hyperthyroidism	Normal	Normal or high	Normal or high
Euthyroid Hyperthyroidism	Normal	Normal or low	Normal or low
Euthyroid Hyperrthyriodmine therapy	Normal	low	Normal or high
euthyroid: thyroid extract therapy	Normal	low normal or low	Normal or high
primary hypothyroidism	High	Low	Normal or low
Subclinical hypothyroid	High	Normal	Normal
hyperthyroidism	Low	High or normal	High
Subclinical hyperthyroidism	Low	Normal	Normal
abnormal hypothalamic- pituitary function			
TSH-mediated hyperthyroidism	Normal or high	High	High
central hypothyroidism	Normal or low	low or low-normal	low or normal

- The thyroid receptor is found in the **nucleus**
- All thyroid disorders are best tested first with a **TSH**
- The most used thionamides are : PTU & methimazole
- PTU inhibit synthesis of T4 + block peripheral conversion of T4 to T3
- methimazole inhibit synthesis of T4, more potent than PTU

MCQ's

Q1: A 60-year-old woman presents to a physician complaining of swelling in her neck. Her past medical history is significant for rheumatoid arthritis and Sjogren syndrome. Physical examination reveals a mildly nodular, firm, rubbery goiter. Total serum thyroxine (T4) is 10 mg/dL, and third-generation thyroid-stimulating hormone (TSH) testing shows a level of 1.2 mIU/mL. Antithyroid peroxidase antibody titers are high, which of the following is the most likely diagnosis?
(A) Euthyroid sick syndrome
(B) Graves disease
(C) Hashimoto thyroiditis
(D) Silent lymphocytic thyroiditis
(E) Subacute thyroiditis

Q2: A 40-year-old woman presents to the physician because of increased nervousness for the past 3 months. She reports insomnia, frequent palpitations without an identifiable cause, and weakness. She has no significant past medical history and takes no medications. Vital signs are remarkable for a blood pressure of 150/60 mm Hg and a pulse of 135/min. She appears anxious, and despite being in the middle of winter, is dressed in a t-shirt and shorts. Physical examination reveals proptosis and eyelid retraction, moist skin, mfid hand tremor, and a palpable diffuse goiter. Which of the following is the most likely diagnosis?
(A) Euthyroid sick syndrome
(B) Follicular carcinoma of the thyroid
(C) Graves disease
(D) Hashimoto thyroiditis
(E) Subacute thyroiditis

Q3 :A 32-year-old woman at 16 weeks' gestation presents to her obstetrician complaining of fatigue, anxiety, and palpitations. She says she has been feeling warm, even in her air-conditioned home, and has been having three or four loose stools per day, as compared to one or two prior to her pregnancy. She has a temperature of 37.1°C (98.9°F), heart rate of 105/min, and blood pressure of 128/76 mmHg. Neck examination reveals mild diffuse enlargement of the thyroid gland with no lymphadenopathy. Relevant laboratory findings include a total triiodothyronine level of 400 ng/dL, free thyroxine of 6.8 ng/dL, and thyroid-stimulating hormone of 0.01 µU/mL (normal: 0.4–4 µU/L). Results of a thyroid stimulating hormone-receptor antibody test are positive. Which of the following is the most appropriate therapy for this patient?
(A) High-dose iodine therapy
(B) Methimazole
(C) Propylthiouracil
(D) Radioiodine ablation
(E) Surgical resection

Q4 :A 16-year-old girl presents to her GP complaining of a swelling in her neck which she has noticed in the last 2 weeks. She has felt more irritable although this is often transient. On examination, a diffuse swelling is palpated with no bruit on auscultation. The most likely diagnosis is:
A. Hyperthyroidism
B. Simple goitre
C. Riedel's thyroiditis
D. Thyroid carcinoma
E. Thyroid cyst

Answers: 1.C, 2.C, 3.C, 4.B

Thank you

If you have any question please contact with us at:
Internalmedicineteam434@gmail.com